

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or Agent's file reference	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR 03/03651	International filing date (day/month/year) 10.12.2003	Priority date (day/month/year) 10.12.2002
International Patent Classification (IPC) or national classification and IPC A61K35/78		
Applicant ROCHE CONSUMER HEALTH LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets including this title page.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Instruction 607 of Administrative Instructions of the PCT).

These annexes consist of a total of          sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement according to Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 01.07.2004	Date of completion of this report 17.03.2005
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JC20 Rec'd PCT/PTO 08 JUN 2005

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## I. Basis of the report

1. This report has been drawn up on the basis of the following elements (*the replacement sheets received by the receiving office in response to an invitation according to Article 14 are considered in the present report as "originally filed" and are not annexed to the report as they contain no amendments (Rules 70.16 and 70.17).):*

## Description, pages:

1-50 as originally filed

## Claims, No.:

1-23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

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5. ☐ This report has been written disregarding (some of) the amendments, which were considered as going beyond the description of the invention, as filed, as is indicated below (Rule 70.2(c)):

*(All replacement sheets comprising amendments of this nature should be indicated in point 1 and attached to this report).*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty	Yes:	Claims	1-23
	No:	Claims	
Inventive Step	Yes:	Claims	1-23
	No:	Claims	
Industrial Applicability	Yes:	Claims	1-23
	No:	Claims	

2. Citations and explanations

**see separate sheet**

**V. Reasoned statement regarding novelty, inventive step and industrial applicability.**

Reference is made to the following documents:

- D1: DATABASE WPI Section Ch, Week 199239 Derwent Publications Ltd., London, GB; Class B04, AN 1992-321310 XP002251031 & KR 9 102 518 B (DONG KUK PHARM CO) April 23, 1991 (1991-04-23).  
D2: EP-A-0 867 447 (DONG KOOK PHARM CO LTD) September 30, 1998 (1998-09-30).  
D3: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1992, COLLINS D J ET AL: "TRITERPENE ACIDS FROM SOME PAPUA NEW GUINEA TERMINALIA SPECIES" XP002251030 Database accession no. PREV199293116315

**Novelty**

D1 and D2 disclose methods for extraction from the plant *Centella asiatica*, that differ from the methods claimed in claims 1 and 2 (at least) by virtue of the absence of steps c) and e). Document D3 concerns ether extracts and is not therefore considered to be relevant.

The description does not cite any documents that reflect the state of the art described on page 3, lines 16-23 (contrary to R.5.1 a)ii) PCT). This prior art concerns methods of extraction for obtaining a mixture of asiaticoside, madecassoside and by-products (15%) or else 81% of madecassoside and close isomers of madecassoside.

The subject matter of claims 1 and 2 relates to methods for preparing an extract of *Centella asiatica* comprising, inter alia, madecassoside and terminoloside. Terminoloside is a positional isomer of madecassoside (present description, p. 4, l. 15). Given that the methods mentioned above comprise a not insignificant amount of impurities, which could be terminoloside because of its structure close to madecassoside. In the absence of any precise further information regarding the various steps of the methods of the prior art and the content of the extracts obtained with said methods, in particular the presence of amounts of terminoloside, the subject matter of claims 1 and 2 is considered to be novel.

The same reservations are expressed for the product claims (claims 9, 12, 15 and 22). As regards the novelty of the product claims 9, 12, 15 and 22, it should be noted that document D3 (summary, final sentence) casts a doubt concerning the presence of terminolic acid glycosides in extracts of *Centella asiatica* and contradicts the passage on p. 4, l. 15-17 ("terminoloside has never been mentioned as being a possible extract of *Centella asiatica*"). For these

reasons, the subject matter of claims 9, 12, 15 and 22 can be considered to be novel.

*Inventive step*

Taking documents D1 and D2, or else the references mentioned on p. 3, l. 16-23 of the present description, to be the closest state of the art, the difference between the extraction methods of the prior art and the invention as claimed would seem to be the presence of terminoloside. The technical problem to be solved is defined as the provision of methods for extracting terminoloside.

Given that D3 casts a serious doubt over the presence of terminolic acid in extracts of *Centella asiatica* and that it is necessary to modify two steps of the method compared with the extraction methods described in D1 and D2, the subject matter of claims 1 and 2 can be considered to be inventive.

The presence of terminoloside in extracts of *Centella asiatica* (that comprise, inter alia, madecassoside and asiaticoside as active agents), has a technical effect (see p. 46 and 48, describing the effects on the production of IL-1 and PGE-2). It ensues that, not only can the method be considered to be inventive, but also the product thus obtained. The subject matter of claims 9, 12, 15, 22 and 23 therefore also involves an inventive step.